


VERTEX

THE SCIENCE *of* POSSIBILITY

SECOND-QUARTER 2021 FINANCIAL RESULTS

JULY 29, 2021

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AGENDA

Introduction

Michael Partridge, Senior Vice President, Investor Relations

CEO Perspective and Pipeline Update

Reshma Kewalramani, M.D., CEO and President

Commercial Update

Stuart Arbuckle, Executive Vice President and Chief Commercial and Operations Officer

Financial Results

Charlie Wagner, Executive Vice President and Chief Financial Officer

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SAFE HARBOR STATEMENT & NON-GAAP FINANCIAL MEASURES

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, the information provided regarding future financial performance and operations, the section captioned "Full-Year 2021 Updated Financial Guidance" and statements regarding (i) anticipated regulatory filings, data availability, approvals, and timing thereof, (ii) anticipated future label expansions, (iii) the expectations, development plans and anticipated timelines for the company's therapies and pipeline programs, including study designs, clinical site activations, patient enrollment, data availability, and timing thereof, (iv) expectations for the collaborations with CRISPR, including expectations regarding achievement of target enrollment in the CTX001 clinical studies, anticipated benefits of the collaborations, the potential of CTX001 to be a one-time functional cure for patients with TDT and SCD, and the possibility of regulatory filings in the next 18-24 months, (v) expectations for uptake of and expanded access to the company's medicines, including additional reimbursement agreements and approvals, (vi) expectations for continued growth in the number of CF patients treated with our medicines, including expectations about our ability to treat up to 90% of CF patients with CFTR modulators, (vii) expectations for our pain program, including our plans to advance VX-548 into Phase 2 acute pain abdominoplasty study and expectations for data from the Phase 2 acute pain bunionectomy study, (viii) expectations for availability of initial data from the VX-880 study, (ix) beliefs about commercial opportunities and operations in the disease areas in which we focus, and (x) expectations for our CF pipeline program, including plans to initiate Phase 3 studies of the next-in-class, once-daily triple combination and the potential of the new triple combination to provide enhanced benefit for people with CF. While Vertex believes the forward-looking statements contained in this presentation are accurate, these forward-looking statements represent the company's beliefs only as of the date of this presentation and there are a number of risks and uncertainties that could cause actual events or results to differ materially from those expressed or implied by such forward-looking statements. Those risks and uncertainties include, among other things, that the company's expectations regarding its 2021 product revenues, expenses and effective tax rates may be incorrect (including because one or more of the company's assumptions underlying its expectations may not be realized), that COVID-19 may have different or more significant impacts on the company's business or operations than the company currently expects, that data from preclinical testing or early clinical trials, especially if based on a limited number of patients, may not be indicative of final results, that the company may not realize the anticipated benefits from our collaborations with third parties, that data from the company's development programs may not be available on expected timelines, or at all, support registration or further development of its potential medicines due to safety, efficacy or other reasons, and other risks listed under Risk Factors in Vertex's annual report filed with the Securities and Exchange Commission and available through the company's website at www.vrtx.com and on the SEC's website at www.sec.gov. You should not place undue reliance on these statements. Vertex disclaims any obligation to update the information contained in this presentation as new information becomes available.

In this presentation, Vertex's financial results and financial guidance are provided in accordance with accounting principles generally accepted in the United States (GAAP) and using certain non-GAAP financial measures. In particular, non-GAAP financial results and guidance exclude from Vertex's pre-tax income (i) stock-based compensation expense, (ii) revenues and expenses related to collaborative milestones and upfront payments, including the $900 million upfront payment to CRISPR, (iii) gains or losses related to the fair value of the company's strategic investments, (iv) increases or decreases in the fair value of contingent consideration, (v) acquisition-related costs and (vi) other adjustments. The company's non-GAAP financial results also exclude from its provision for income taxes the estimated tax impact related to its non-GAAP adjustments to pre-tax income described above and certain discrete items. These results should not be viewed as a substitute for the company's GAAP results and are provided as a complement to results provided in accordance with GAAP. Management believes these non-GAAP financial measures help indicate underlying trends in the company's business, are important in comparing current results with prior period results and provide additional information regarding the company's financial position that the company believes is helpful to an understanding of its ongoing business. Management also uses these non-GAAP financial measures to establish budgets and operational goals that are communicated internally and externally, to manage the company's business and to evaluate its performance. The company adjusts, where appropriate, for both revenues and expenses in order to reflect the company's operations. The company's calculation of non-GAAP financial measures likely differs from the calculations used by other companies. The company provides guidance regarding combined R&D and SG&A expenses and effective tax rate on a non-GAAP basis. The guidance regarding combined GAAP R&D and SG&A expenses does not include estimates associated with any potential future business development activities. The company does not provide guidance regarding its GAAP effective tax rate because it is unable to forecast with reasonable certainty the impact of excess tax benefits related to stock-based compensation and the possibility of certain discrete items, which could be material. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the appendix hereto and in the company's Q2 2021 press release dated July 29, 2021.

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VERTEX Q2 2021:

Outstanding financial performance driven by our continued **leadership in CF;** multiple **pipeline programs advancing** through all stages of clinical development

Leadership in CF

- TRIKAFTA/KAFTRIO positioned to address 90% of CF patients
- New approvals and reimbursement agreements across our CF portfolio
- Next-in-class combination regimen advancing to Phase 3 in 2H 2021

Pipeline Programs Advancing

- Broad clinical pipeline spans 5 diseases outside CF and 3 therapeutic modalities
- Progress is accelerating across the portfolio
- Potential for multiple clinical data readouts in the next 6 to 9 months

Revenue Growth

- $1.8B in Q2 ’21 revenues, an ~18% increase compared to prior year
- 2021 product revenue guidance raised by $500M to a range of $7.2-$7.4B
- Ended the quarter with $6.7B in cash, following the $900M payment for the amended CRISPR collaboration

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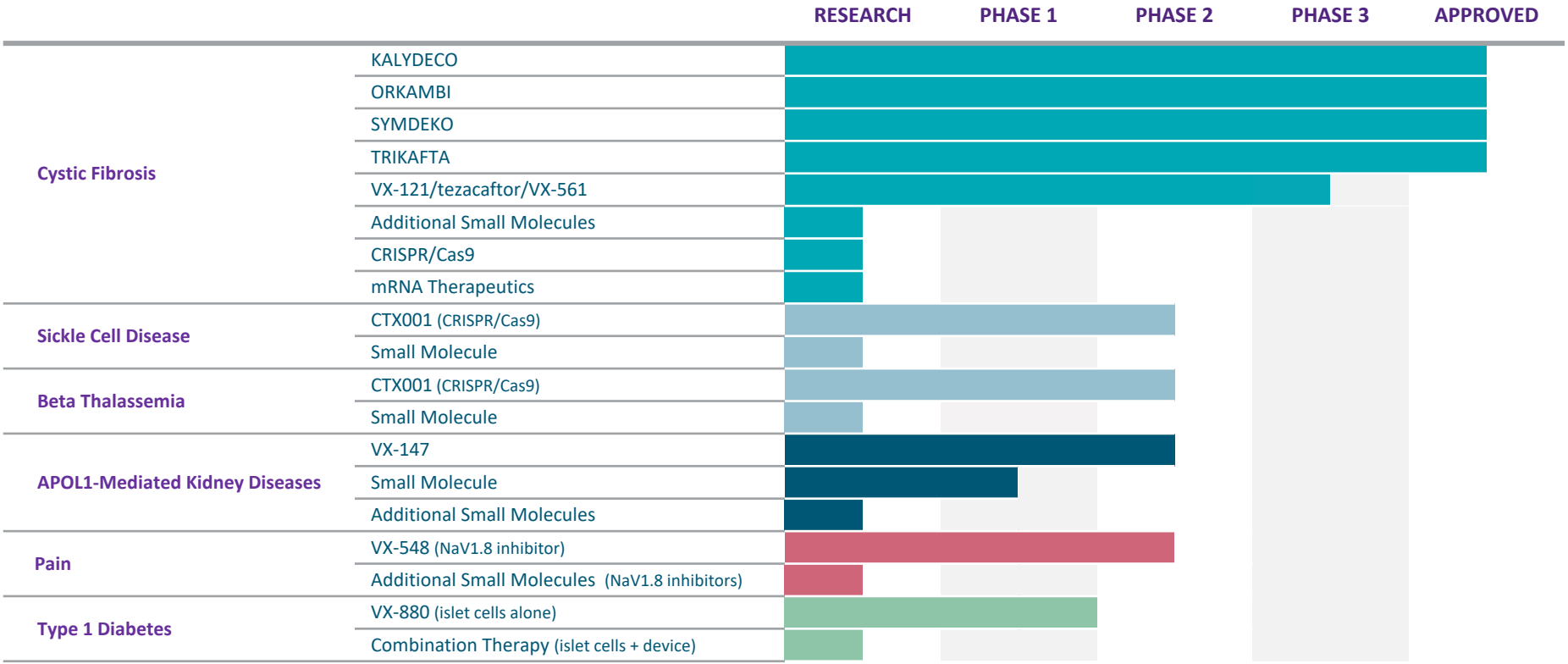
PROGRAMS IN MULTIPLE DISEASE AREAS ACTIVE IN CLINICAL DEVELOPMENT WITH POTENTIAL FOR DATA READOUTS IN THE NEXT 6 TO 9 MONTHS



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VX-121/TEZACAFTOR/VX-561, THE NEXT-IN-CLASS TRIPLE COMBINATION REGIMEN, WILL BE EVALUATED IN TWO 48-WEEK PHASE 3 PIVOTAL CLINICAL TRIALS

F = F508del
MF = Minimal Function
F/F+ = F/F, F/Gating, F/Residual Function

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MULTIPLE POTENTIALLY TRANSFORMATIVE PROGRAMS OUTSIDE OF CF

SMALL MOLECULES

APOL1-Mediated Kidney Diseases
VX-147 in Phase 2

Potential POC data in APOL1-mediated FSGS on-track for 2H21

NaV1.8 inhibitor for Pain
VX-548 in Phase 2

Two studies in acute pain (bunionectomy and abdominoplasty) with opioid reference arm; first data anticipated by early 2022

Alpha-1 Antitrypsin Deficiency

One or more small molecules expected to enter the clinic in 2022

CELL AND GENETIC THERAPIES

Sickle Cell Disease & Beta Thalassemia
CTX001 in Phase 2

- More than 45 patients dosed across two studies
- Expect to achieve target enrollment in both studies in Q3
- Anticipate filing for approval in the next 18-24 months

Type 1 Diabetes
Phase 1/2 underway with VX-880

- First patient dosed with VX-880 in the "islet cells alone" program
- Cells + device program progressing in late preclinical studies

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ON THE PATH TO TREATING UP TO 90% OF CF PATIENTS WITH CFTR MODULATORS

TRIKAFTA

- Vast majority of patients eligible for TRIKAFTA ages 12+ with at least one *F508del* mutation in the U.S. have initiated TRIKAFTA therapy
- Persistence and compliance levels continue to be high
- Strong start to the launch of TRIKAFTA in children ages 6-11 following approval in June 2021

KAFTRIO

- KAFTRIO approved for people ages 12+ with at least one *F508del* mutation in the EU
- Strong uptake across multiple key countries where patients have access
- Multiple reimbursement agreements reached, including France and Italy, less than 1 year after EMA approval
- Regulatory submission filed in Europe for children ages 6-11

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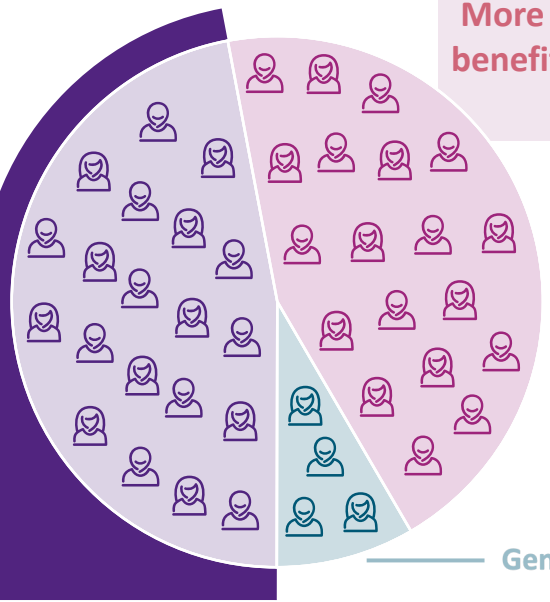
OPPORTUNITY FOR FURTHER SUBSTANTIAL GROWTH IN CF

83,000 people with CF in U.S., Europe, Australia and Canada

~50% of Patients Currently Treated with Vertex Medicines



More than 30,000 patients who could benefit from CFTR modulators who are not yet being treated

Genetic Therapies Needed

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SIGNIFICANT NEAR-TERM CTX001 MARKET OPPORTUNITY WITH A GEOGRAPHICALLY CONCENTRATED PATIENT POPULATION

More than 150,000

Total SCD & BT patients in the U.S. & EU

~32,000

Severe SCD & BT patients in the U.S. & EU

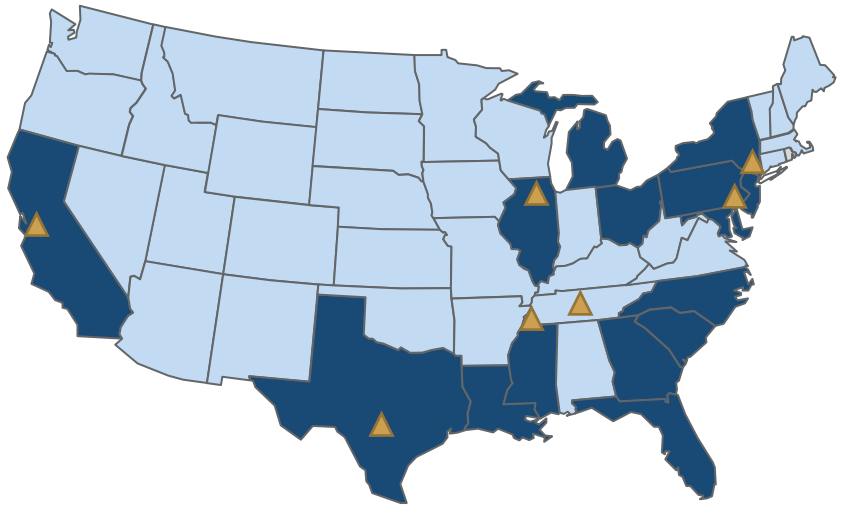
~25,000

Severe SCD patients in the U.S. & EU, the vast majority in the U.S.

Concentrated Treatment Landscape

15 States Account for **~75%** of SCD Patients

▲ Current CTX001 Clinical Trial Sites



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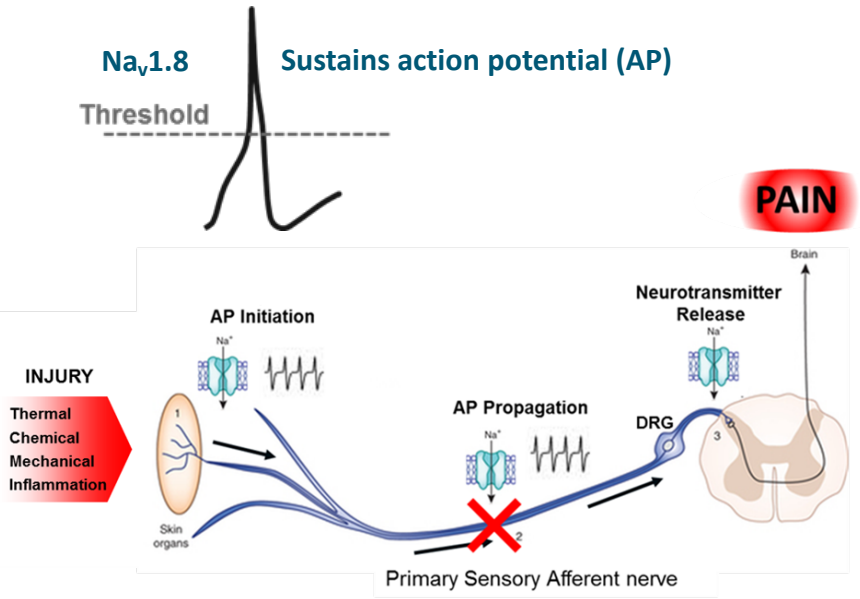
ACUTE PAIN IS A SIGNIFICANT MARKET OPPORTUNITY THAT CAN BE SERVED WITH A SMALL COMMERCIAL FOOTPRINT

There is a **need for new pain medicines** without the limitations of opioids, particularly their addictive potential

Acute pain is estimated to be a **$4B market** despite 90% of prescriptions being generic

Treatment is **highly concentrated** where 25% of hospitals account for 80% of the opioid prescriptions in the U.S.



From Waxman and Zamponi, Nature Neuroscience, 2014

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Q2 2021 FINANCIAL HIGHLIGHTS

($ in millions except as noted, per share data and percentages)	Q2 20	FY 20	Q2 21
Total CF product revenues	$1.52B	$6.20B	**$1.79B**
TRIKAFTA/KAFTRIO	918	3.86B	**1.26B**
SYMDEKO/SYMKEVI	172	629	**134**
ORKAMBI	232	908	**221**
KALYDECO	203	803	**183**
Combined non-GAAP R&D and SG&A expenses	467	1.98B	**537**
Non-GAAP operating income	874	3.49B	**1.03B**
Non-GAAP operating margin	57%	56%	**57%**
Non-GAAP net income	687	2.72B	**811**
Non-GAAP net income per share - diluted	$2.61	$10.32	**$3.11**
Cash, cash equivalents & marketable securities (period-end)	$5.5B	$6.7B	**$6.7B**

Notes: An explanation of non-GAAP financial measures and reconciliation of combined non-GAAP R&D and SG&A expenses, non-GAAP operating income and non-GAAP net income to corresponding GAAP measures are included in the company's Q2 2021 press release dated July 29, 2021. Non-GAAP financial measures are presented compared to corresponding GAAP measures in the appendix of this presentation. Totals above may not add due to rounding.

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FULL-YEAR 2021 UPDATED FINANCIAL GUIDANCE

	Current FY 2021 Guidance	Previous FY 2021 Guidance	FY 2021 Commentary
Total CF Product Revenues	**$7.2 - $7.4B**	$6.7 - $6.9B	$500M increase based on performance YTD and new reimbursement agreements
Combined GAAP R&D and SG&A Expenses	**Unchanged**	$2.9 -$3.05B	
Combined Non-GAAP R&D and SG&A Expenses	**Unchanged**	$2.25 -$2.3B	
Non-GAAP Effective Tax Rate	**Unchanged**	21-22%	

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Note: An explanation of non-GAAP financial measures and a reconciliation between the company's full-year 2021 combined GAAP R&D and SG&A expenses and combined non-GAAP R&D and SG&A expenses guidance is included in the company's Q2 2021 press release dated July 29, 2021.


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APPENDIX

GAAP TO NON-GAAP FINANCIAL INFORMATION

($ in millions except as noted, per share data and percentages)	Q2 20	FY 20	Q2 21
Combined R&D and SG&A expenses			
GAAP	613	**2.60B**	1.60B
Non-GAAP	467	**1.98B**	537
Operating income			
GAAP	718	**2.86B**	(38)
Non-GAAP	874	**3.49B**	1.03B
Operating Margin %:			
GAAP	47%	**46%**	(2%)
Non-GAAP	57%	**56%**	57%
Net income			
GAAP	837	**2.71B**	67
Non-GAAP	687	**2.72B**	811
Net income per share - diluted			
GAAP	$3.18	**$10.29**	$0.26
Non-GAAP	$2.61	**$10.32**	$3.11

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Note: An explanation of non-GAAP financial measures and reconciliation of combined non-GAAP R&D and SG&A expenses, non-GAAP operating income and non-GAAP net income to corresponding GAAP measures are included in the company's Q2 2021 press release dated July 29, 2021.